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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,056	06/22/2001	Kenneth Kornman	MSA-023.01	6975

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,056	KORNMAN ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9-16,18-23,26,27,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, 9-16, 18-23, 26, 27, 38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

FINAL ACTION

1. Applicant's amendment filed June 1, 2004 is acknowledged and has been entered. Claims 1, 5 16 and 20 have been amended. Claims 2, 8, 17, 24-25 and 28-37 have been canceled. Claims 38 and 39 have been added. Claims 1, 3-7, 9-16, 18-23, 26-27 and 38 and 39 are pending. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the new grounds of rejections necessitated by Applicant's amendment of the claims and submission of new claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The claim rejection under 35 USC 112 second paragraph is withdrawn in view of Applicant arguments. The prior art rejection under 35 USC 102 is withdrawn in view of Applicant's amendment.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3-7, 9-16, 18-23, 26-27, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "a method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject.... by observing in a test subject having an inflammatory disease-associated genotype comprising at least one inflammatory disease-associated allele from the IL-1 44112332 haplotype cluster or the IL-1 33221461 haplotype cluster, a biomarker....", it does not reasonably provide enablement for "a method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject.... by observing in a test subject having an inflammatory disease-associated genotype comprising at least one inflammatory disease-associated allele selected from the group consisting of an IL-1A allele, an Il-1B allele, an IL-1RN allele, a TNF-A allele and an IL-13 allele, a biomarker..." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The first paragraph of section 112 requires the specification describe how to make and use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is "undue". These factors include but are not limited to: (1) quantity of experimentation necessary, (2) the amount of direction or guidance presented in the specification, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the

unpredictability of the art and (8) the breadth of the claims. (See *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404, (Fed. Cir. 1988)) *(MPEP 2164.01(a))*.

The claimed invention is drawn to a method for identifying a substance that is likely to prevent or diminish a specific biological response in a subject having an inflammatory disease-associated genotype wherein one of the method steps comprises observing in a test substance having an inflammatory disease-associated genotype comprising at least one inflammatory disease-associated allele-selected from the group consisting of an IL-1A allele, an IL-1B allele, an IL-1RN allele, a TNF-A allele and an IL-13 allele, a biomarker. The claims broadly encompass any allele in the IL-1A gene, any allele in the IL-1B gene, any allele in the IL-1RN allele, any allele in the TNF A gene and any allele in the IL-13 allele. The specification however does not support the large genus of nucleic acid species encompassed by the claims. The specification in section 5.2 and the examples discloses the identification of the inflammatory disease-associated alleles associated with the instant method by representation of two different haplotypes. The specification at page 12 discloses that the IL-1 44112332 haplotype comprises the following alleles: allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of the IL-1 A, allele 1 of the -889 marker of the of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 2 of the VNTR marker of IL-1RN. The specification at page 13 discloses that the IL-1 33221461 haplotype comprises the following alleles: allele 3 of the 222/223 marker of Il-1A, allele 3 of the gz5/gz6 marker of the IL-1 A, allele 2 of the -889 marker of the of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL_1B, allele 4 of the gaat.p33330 marker, allele 6

of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, allele 1 of the VNTR marker of IL-1RN and allele 2 of + 6912 of IL-1B. The specification at page 14, Table 1, identifies association of the identified alleles from the two haplotypes with certain inflammatory diseases.

The specification however, fails to provide any disclosure or evidence for identification and association of any inflammatory diseases-associated allele or markers from the IL-1A gene, IL-1B gene, IL-1RN gene, TNF-A gene and IL-13 gene as encompassed by the claims. There are is no guidance or working examples which indicates that any allele from the IL-1A gene, IL-1B gene, IL-1RN gene, TNF-A gene and IL-13 gene or haplotypes encompassing any allele from those genes are functional in a method for identifying a substance that is likely to prevent or diminish a specific biological response. In fact, it is unpredictable that any and every allele from the IL-1A gene, IL-1B gene, IL-1RN gene, TNF-A gene and IL-13 gene as claimed in the instant invention is indicative of an inflammatory-disease associated genotype given the large sizes of the different genes. For example, the art teaches that the size of the IL-1A gene is about 11.48Kb and encompasses 7 exons (see GENATLAS: Gene Database, http://www.dsi.univ-paris5.fr/genatls/fiche.php?symbol=IL1A, last updated 23/02/2004). Thus, one could not predict without further undue experimentation which inflammatory disease and inflammatory disease-associated genotype(s) are effective in identifying a substance that may be capable of preventing or diminishing a biological response associated with the desired disease. Additionally, as indicated by Applicant's specification, different inflammatory diseases have different associations with different IL alleles. However, there is no disclosure in the specification that would allow one to

assume that any IL allele or TNF allele from any of the IL-1A gene, IL-1B gene, IL-1RN gene, TNF-A gene and IL-13 gene would be associated with an inflammatory disease and thus elicit a diseased phenotype. In fact, the art teaches the association of several alleles of TNF-A which are encompassed by the instant invention with endometriosis (see Asghar et al., Human Reproduction, vol. 19, no. 11, pages 2509-14, 2004). Therefore, undue experimentation is deemed necessary for one of skill in the art to obtain the claimed invention.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-7, 9-16, 18-23, 26-27, 38 and 39 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims as written encompass a large genus of nucleic acid species not adequately described or disclosed in the recitation of "at least one inflammatory disease-associated allele selected from the group consisting of an IL-1A allele, an IL-1B allele, an IL-1RN allele, a TNF-A allele and an IL-13 allele". The specification as filed only discloses the identification of two haplotypes that encompasses alleles 3 and 4 of the 222/223 marker of IL-1A, alleles 3 and 4 of the gz5/gz6 marker of the IL-1 A, alleles 1 and 2 of the -889 marker of the of IL-

1A, alleles 1 and 2 of the +3954 marker of IL-1B, alleles 3 and 4 of the gaat.p33330 marker, alleles 3 and 6 of the y31 marker, alleles 1 and 2 of +2018 of IL-1RN, alleles 1 and 2 of +4845 of IL-1A, alleles 1 and 2 of the VNTR marker of IL-1RN, allele 1 of the -511 marker of IL-1B and allele 2 of + 6912 of IL-1B. The specification provides insufficient written description to support the large genus of nucleic acid species encompassed by the claimed invention.

A representative number of nucleic acid species for each genus must be disclosed to meet the written description requirement of 112, first paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date Applicant was in possession of the claimed invention. Absent a written description disclosing a representative number of the species as claimed in claims 1, 3-7, 9-16, 18-23, 26-27, 38 and 39 of the specification fails to show that Applicant was, in fact "in possession of the claimed invention" at the time the application for patent was filed.

Conclusion

8. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

8/30/05